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Title: Constraint-Induced Aphasia Therapy versus Intensive Semantic Treatment in fluent aphasia

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ABSTRACT

- Objective: To compare the effectiveness of two intensive therapy methods: Constraint-Induced Aphasia Therapy (CIAT) and semantic therapy (BOX).
- Method: Nine patients with chronic fluent aphasia participated in a therapy programme to establish behavioral treatment outcomes. Participants were randomly assigned to one of two groups (CIAT or BOX).
- Results: Intensive therapy significantly improved verbal communication. However, BOX treatment showed a more pronounced improvement on two communication measures, namely on a standardized assessment for verbal communication, the Amsterdam Nijmegen Everyday Language Test (Blomert, Koster, & Kean, 1995) and on a subjective rating scale, the Communicative Effectiveness Index (Lomas et al., 1989). All participants significantly improved on one (or more) subtests of the Aachen Aphasia Test (Graetz et al., 1992), an impairment-focused assessment. There was a treatment-specific effect. Therapy with BOX had a significant effect on language comprehension and on semantics, while of CIAT affected language production and phonology.
- Conclusion: The findings indicate that in patients with fluent aphasia (1) intensive treatment has a significant effect on language and verbal communication, (2) intensive therapy results in selective treatment effects and (3) an intensive semantic treatment shows a more striking mean improvement on verbal communication in comparison to communication-based CIAT-treatment.

1. INTRODUCTION

There has been increasing evidence that short term, intensive aphasia therapy in the chronic stages of aphasia recovery has a beneficial effect irrespective of the type of treatment. However, it is not clear what the optimal therapy content, intensity and setting may be to deliver aphasia therapy across a variety of aphasia profiles in terms of aphasia severity, aphasia type/linguistic impairment, recovery stage and lesion site (for a review see Robey, 1998; Basso, 2005; Berthier, 2005; Brady, Kelly, Godwin & Enderby 2012). Aphasia therapies can either be based on a cognitive linguistic approach (Patterson & Shewell, 1987) or a communicative approach (Davis & Wilcox, 1985; Holland, 1991).

The cognitive linguistic approach is based on the theoretical framework of cognitive neuropsychology (Ellis & Young, 1996). In this approach aphasia therapies focus on the language deficit itself in order to restore the linguistic processes involving semantics, phonology, morphology and syntax. The improvement of linguistic skills will also improve patients' verbal communication ability (Visch-Brink, Bajema & Van de Sandt-Koenderman, 1997; Doesborgh et al., 2004; Whitworth, Webster & Howard, 2005). An example of a cognitive linguistic therapy is the Dutch drill-based lexical-semantic therapy programme BOX (Visch-Brink & Bajema, 2001).

While the cognitive linguistic approach focuses on the language deficit, the emphasis of the communicative approach is on the communicative aspects of language. Important issues in this perspective are the compensation strategies in communicative settings and the application of residual skills in communication (Holland, 1991; Croteau & Le Dorze, 2006; Simmons-Mackie, Kearns & Potechin, 2005). A typical communicative based approach is 'Promoting Aphasic Communicative Effectiveness' (PACE: Davis & Wilcox, 1985): patients are

permitted to communicate in any and all modalities (e.g. gesturing, pointing, writing) throughout the therapy session.

A communicative therapy which is currently gaining ground is 'Constraint-Induced Aphasia Therapy' (CIAT). The main difference between PACE and CIAT is the availability of alternative methods to support communication. CIAT is based on work which explores the use of constraint-induced movement therapy in the rehabilitation after stroke (Taub, Uswatte & Pidikiti, 1999). These studies have shown that motor behavior of an impaired limb can be modified by a short period of intensive constraint practice (Meinzer, Rodriguez, Gonzalez & Rothi, 2012; for a review see Taub et al., 1999; Taub, Uswatte & Elbert, 2002).

Constraint-Induced Aphasia Therapy was introduced in 2001 in a randomized clinical trial with 17 chronic aphasia patients (Pulvermüller et al., 2001). CIAT is also known as CIAT plus (Meinzer, Djundja, Barthel, Elbert & Rockstroh, 2005), Constraint-Induced Language Therapy (CILT; Maher et al., 2006) or Intensive Language Action Therapy (ILAT; Pulvermüller & Berthier, 2008). This programme consists of four major components: (1) massed practice (30 to 35 hours of speech therapy in two weeks), (2) shaping of responses (gradually increasing task and stimulus complexity), (3) constraint of compensatory (non-verbal) communication strategies and (4) socially driven communication tasks (therapy tasks involving interaction-based games) (DiFrancesco, Pulvermüller & Mohr, 2012).

Although CIAT is appropriately defined as a communication-based approach, some elements of cognitive linguistic treatment might be incorporated in relation to the shaping of the patient's responses. But the main aspect of CIAT is the communicative load, since it involves the exchange of new information between participants in dialogues (Hengst, Duff & Dettmer,

2010). CIAT does not only improve verbal communication, but also leads to a clinical improvement of language functions as it might entail the re-learning of word-concept links and the re-wiring of neuronal connections in language networks (Difrancesco et al., 2012).

The introduction of constraint-induced (CI) principles in aphasia rehabilitation has also created a renewed interest in issues like therapy intensity and massed practice (Bhogal, Teasell & Speechley, 2003; Basso, 2005; Hinckley & Carr, 2005; Raymer et al., 2008). The beneficial effect of an intensive treatment in the chronic stage of aphasia is consistent with recent work in neuroscience which supports several principles of experience-dependent neural plasticity in the rehabilitation after brain injury, including sufficient treatment intensity and the forced use of cognitive capacities (Raymer et al., 2008; Kleim & Jones, 2008; Barthel, Meinzer, Djundja & Rockstroh, 2008). Robey (1998) carried out a meta-analysis of the effect of treatment intensity and concluded that there is a clear relationship between therapy intensity and the degree of improvement. Raymer et al. (2008) emphasized the need for systematic research into the optimal aphasia therapy. Standard therapy or different forms of communicative therapy also seem to benefit from more intense application (Maher et al., 2006; Barthel et al., 2008). Thus, the effectiveness of a short-term intensive treatment over a restricted period has been demonstrated in chronic aphasia patients regardless of the type of treatment (for a review see, Cherney, Patterson, Raymer, Frymark and Schooling, 2008).

There have been a large number of studies which focus on the treatment of patients with nonfluent aphasia (e.g. Fridriksson et al., 2012; Links, Hurkmans & Bastiaanse, 2010; Conley & Coelho, 2003). However, studies on patients with fluent aphasia are rare. There is no proven method for the rehabilitation of fluent aphasia (Altschuler, Multari, Hirstein & Ramachandran, 2006). One of the reasons might be the frequently observed anosognosia in

patients with Wernicke aphasia, a problematic factor in relation to a systematic linguistic treatment. Another factor might be the great variation in the underlying linguistic disorders. Robson, Sage and Lambon Ralph (2012) propose three hypotheses to account for the comprehension impairment in fluent aphasia: (1) disruption of acoustic and/or phonological analysis (e.g. Moses, Nickels & Sheard, 2004); (2) semantic impairment (e.g. Butterworth, 1992); or (3) a combined phonological-semantic impairment, i.e. the dual hypothesis (e.g. Hillis, Boatman, Hart & Gordon, 1999). Treatment of subjects with fluent aphasia can therefore focus on semantics, phonology or even syntax (e.g. Boyle, 2004; Edwards & Tucker, 2006; Sampson & Faroqi-Shah, 2011). The disproportionate representation of nonfluent aphasia is also characteristic for CIAT studies. In an evidence-based review of the treatment intensity effects in constraint-induced language therapy, Cherney et al. (2008) indicated that most of the participants in CIAT studies were nonfluent (60%, 42 of 70) and therefore it is questionable whether the results can be generalized to patients with fluent aphasia. Evidence from a cognitive linguistic approach has shown that specific treatment of a disturbed language level can have a significant impact on verbal communication, i.e. the ability to bring the message across in speech (Doesborgh et al., 2004). From CIAT literature evidence has shown that intensive treatment in a chronic aphasia population can augment conversational skills (Cherney et al., 2008). Therefore we want to explore the relevance of both approaches in fluent aphasia: CIAT and cognitive linguistic treatment.

The objective of this study is to investigate the effectiveness of two intensive therapy programmes in patients with chronic fluent aphasia after stroke: (1) a cognitive linguistic therapy, i.e. an individualized drill-based lexical-semantic treatment using the Dutch therapy programme BOX (Visch-Brink & Bajema, 2001) and (2) CIAT, i.e. a more communication-based group treatment focusing on verbal communication using constraints (Pulvermüller et

al., 2001). It is predicted that a pure semantic treatment with BOX will have a selective favorable influence on verbal semantic performance and that verbal communication skills will be enhanced at activity level (Doesborgh et al., 2004), because of an improved verbal semantic processing in everyday language. It is further predicted that a treatment with CIAT will not only have a positive effect on patients' verbal communication skills, but will also create significant improvement at different linguistic levels (i.e. semantics and phonology). Since CIAT in its nature is an oral communication based treatment focusing on language production as well as language comprehension, it is reasonable to predict that it would have a positive effect on multiple levels of verbal communication. Consequently it is expected that verbal communication, measured by a standardized assessment as well as by a subjective rating scale, will improve after both treatment methods.

2. METHOD and PROCEDURE

2.1 Participants

The present study is an exploratory study in which participants with fluent aphasia were randomly assigned to CIAT (Pulvermüller et al., 2001) or BOX (Visch-Brink & Bajema, 2001) (for more details see Appendix).

The participants in this study were 9 native speakers of Belgian Dutch (Verhoeven, 2005) with a mean age of 66.8 years (SD ± 9.2 years, range 54 to 81 years) and chronic vascular fluent aphasia (mean duration 56.9 months, SD ± 37.7 months, range 17 to 138 months). Participants were recruited on the basis of the following inclusion criteria: (1) adult age; (2) single and first ever stroke in the left hemisphere confirmed by structural brain imaging; (3) moderately impaired language function and; (4) fluent aphasia with a combined semantic and phonological deficit. The impairment of language functions was determined on the basis of

the Stanine-norms on the Token Test (TT) of the Dutch version of the Aachen Aphasia Test (AAT: Graetz, de Bleser & Willmes, 1992). The criterion for a semantic deficit was a score below two standard deviations (SD) on at least one of the following semantic tasks: (1) AAT-Comprehension (AAT: Graetz et al., 1992); (2) Verbal Semantic Association Test (SAT: Visch-Brink, Stronks & Denes, 2005); (3) Psycholinguistic Assessment of Language Processing in Aphasia subtest Synonym Judgment (PALPA: Kay, Coltheart & Lesser, 1992; Dutch version: Bastiaanse, Bosje & Visch-Brink, 1995); or (4) PALPA Semantic Word Association of low imageability words. The criterion for a phonological deficit was a score below two standard deviations (SD) on at least one of the following language tests: (1) AAT-Repetition; (2) PALPA Non-word Repetition; or (3) PALPA Auditory Lexical Decision. Explicitly excluded from this study were patients participating in any other treatment programme, patients with an additional neurological or psychiatric disorder and patients with severe perceptual, additional speech (e.g. verbal apraxia) or cognitive deficits evidenced by formal neuropsychological testing.

The demographic and neurological characteristics of the participants are summarized in Table I.

Insert* Table I *here please

Six participants were diagnosed with Wernicke's aphasia. The aphasia profile of the other three was consistent with a diagnosis of transcortical sensory aphasia. In seven patients, aphasia resulted from a left hemisphere ischemic stroke while two patients had a hemorrhage (see Table I). In addition to the aphasiogenic lesion in the left temporo-parietal region, CT scan of the brain in patient B4 revealed a small cystic lesion in the right parietal lobe with slight attraction of the lateral ventricle. Aphasia symptoms in this patient, however, had

emerged simultaneously with the left temporo-parietal infarction only. Careful examination of the patient's medical history revealed that structural damage in the right parietal region had not resulted in clinically relevant symptoms and the aphasiogenic nature of this old lesion was formally ruled out. Although Meinzer et al. (2005) found no relationship between aphasia severity and the benefit of CIAT treatment, only patients with a moderately impaired language function were included because (1) CIAT requires similar levels of severity in the treatment groups and (2) in view of the small number of participants, a homogeneous aphasia sample was recruited.

2.2 Treatment programmes

CIAT-treatment is a communication-based group interaction by means of communicative card games. The picture cards contain objects of high as well as low frequent words, black-and-white line drawings as well as colored pictures, pictures of objects as well as action cards and pictures with minimal pairs (such as 'sock' and 'rock') (see below 'Participants treatment' and Appendix for more details). The intervention procedure was based on Maher et al. (2006), Meinzer et al. (2005, 2007) and Pulvermüller et al. (2001). In this study, patients were allowed to produce gestures in order to facilitate verbal output, but their gestures were hidden from the other participants by a 40-cm high screen between the patient and the other participants. As a result, gestures could not act as a primary means of communication and participants were encouraged to use their verbal communicative abilities, i.e. verbal expressions and phrases (for more details, see Appendix).

The semantic therapy is a drill-based lexical-semantic treatment using BOX, which is a Dutch therapy programme (Visch-Brink & Bajema, 2001). This programme focuses on the interpretation of written words, sentences and texts (also with an auditory presentation by the speech and language therapist if required). BOX contains a variety of semantic decision tasks

aimed at enhancing semantic processing. There are eight different types of exercises within each task and the patient is required to deny or confirm the semantic relationship between (written and auditorily presented) content words, either presented separately or within the context of a sentence or text (for more details, see Appendix). Word choice, number of distractors, semantic relatedness and ambiguity were taken into account in creating different levels of difficulty (Visch-Brink et al., 1997).

Participants were randomly assigned to one of the above treatments. One group (three women and two men) received communication-based treatment (CIAT), while the other group (four men) received semantic treatment (BOX). The groups did not differ significantly in age ($t(7)=-1.4$, $p=0.214$), aphasia duration ($t(7)=0.4$, $p=0.728$) or education level ($t(7)=-0.7$, $p=0.621$). The group allocation was computer generated and remained concealed in sequentially numbered opaque, sealed envelopes until randomization.

2.3 Intervention

2.3.1 Therapist training

Intervention was administered by seven trained speech and language therapy students (third year professional bachelor level). During the first two days of the training the students remained under the supervision of six experienced and professionally trained speech and language therapists. Students were trained according to the training protocol of laypeople designed by Meinzer et al. (2007). The speech and language therapists had been given detailed instructions by means of a two-hour presentation in which the study was presented. The basic principles of BOX and CIAT were introduced and the materials, procedures and approaches of both types of intervention were carefully explained. In addition, students were given a one-hour practical training session. Instruction sessions contained illustrative video

materials. The students and therapists were given a detailed manual with explicit guidelines about CIAT and BOX. The students and therapists kept a detailed daily record of each intervention, specifying the presence of participants and therapists, the duration of the training in minutes and the training materials used. These records were used for a daily evaluation and critical assessment of each session in order to adjust individual or group task difficulty for the next session.

2.3.2 Participant treatment

All patients received treatment during two- to three-hour sessions per day on nine or ten consecutive working days (total mean duration 1175 minutes, SD ± 64 minutes, pauses not included). There was no significant difference in the amount of treatment between the CIAT group (total mean duration 1195 minutes, SD ± 59 minutes) and the BOX group (total mean duration 1150 minutes, SD ± 69 minutes) in terms of the mean duration of intervention in minutes ($t(7)=1.1$, $p=0.328$). Each session was interrupted by two breaks of 10 to 15 minutes. For the CIAT treatment the dual card game was used, which has been used in prior studies (e.g. Maher, 2006). In this game participants are dealt cards from a set of 32 to 42 colored cards (=16 to 21 pairs of identical cards) per 45 minutes treatment. They take turns either requesting an identical card from the other participant (n=4 to 6 cards per participant) or responding to that request (Faroqi-Shah & Virion, 2009; Breier et al., 2009). Constraints were along three dimensions: (1) difficulty of the material, (2) the rules of the game, as indicated by verbal instruction and shaping and (3) reinforcement contingencies (Pulvermüller et al., 2001) (Table II).

Insert* Table II *here please

The patients in the BOX-group worked alternating (1) by themselves on worksheets and (2) with the therapist according to a therapy schedule (Table II) which allowed one therapist to supervise two patients. For example, on the first day, patient number one started with 30 minutes of therapy (therapy schedule BOX 1) whereas patient number two began with a 30-minute individual working session (therapy schedule BOX 2). The next day participants swapped therapy-schedule. Patients were able to adjust their personal level of difficulty. In order to apply the shaping principle (see Appendix for more details), therapists monitored performance and solicited patient feedback to ensure that patients were challenged but not overly frustrated.

Five intervention groups (two CIAT and three BOX sessions) were formed. Intervention sessions were held at four different hospitals of Ziekenhuis Netwerk Antwerp, i.e. 'Middelheim', 'Jan Palfijn', 'Sint-Erasmus' and CEPOS Duffel: C1, C2 and C3 were treated at 'Middelheim' by two students; C4 and C5 together with another patient with a very mild aphasia were treated at CEPOS by two other students (the last patient was excluded because he scored within normal range on the TT at pretest). The CIAT-groups had the same group members and the same SLT-students throughout the intervention, The BOX participants were individually treated by another three students at 'Middelheim' (B1 and B2), 'Jan Palfijn' (B3) and 'Sint-Erasmus' (B4). The student therapists were supervised by one of the authors, a licensed clinician. Informed consent was obtained from each participant or from a close relative. The study was approved by the local Ethics Committee of Ziekenhuis Netwerk Antwerp.

2.4 Measures

Insert* Tables III *here please

Before entering the study all participants were administered the Raven Colored Progressive Matrices (Raven, 1976) on which they had to obtain a score above the 75th percentile. Handedness was formally assessed by means of a standard handedness inventory (Oldfield, 1971) (Table III). All participants were formally tested at two different time points during the study: before the treatment (pre-test) and one week after treatment to check which therapy condition was the most effective (post-test). The language assessment protocol consisted of: (1) AAT (Graetz et al., 1992); (2) Boston Naming Test [BNT] (Kaplan et al., 1983; Mariën, Mampaey, Vervaet, Saerens & De Deyn, 1998); (3) PALPA (Kay et al., 1992; Dutch version: Bastiaanse et al., 1995); (4) Semantic Association Test [SAT] (Visch-Brink et al., 2005); (5) Amsterdam Nijmegen Everyday Language Test [ANELT] (Blomert, Koster & Kean, 1995); and (6) Communicative Effectiveness Index [CETI] (Lomas et al., 1989) (Table III). Pre- and post-test assessment consisted of an extensive impairment-focused assessment (1-4) together with discourse outcome measures (5-6) because the ultimate aim of aphasia treatment is an improvement of communication rather than a reduction of language impairment (Carragher, Conroy, Sage & Wilkinson, 2012).

The AAT (Graetz et al., 1992) is a standardized comprehensive language battery which consists of five blocks, i.e. the Token Test, Repetition tasks, Written Language tasks, Naming tasks and Comprehension tasks. The test has a high test-retest reliability (two-day interval: retest reliability > .91 for all subtests in chronic aphasia patients (Graetz et al., 1992, p.96)). The AAT was used to obtain a formal description of the individuals' language skills. The BNT (Kaplan et al, 1983; Mariën et al., 1998) is a naming test consisting of 60 line drawings representing objects, animals, food and plants. The test was included in the study since naming is a sensitive outcome measure for linguistic improvement in aphasia (Strauss, Sherman & Spreen, 2006). Subtests of the PALPA (Bastiaanse et al., 1995) and the SAT (Visch-Brink et al., 2005) were added to obtain a more detailed picture of participants'

phonological and semantic abilities. Four PALPA subtests were included, i.e. Synonym Judgment, Semantic Word Association of low imageability words, Non-word Repetition and Auditory Lexical Decision. Two subtests of the SAT were included, i.e. the Visual and Verbal SAT. The ANELT (Blomert et al., 1995) was administered to identify and rate the severity of the verbal communicative deficit. In addition, the quality of verbal communication in everyday life was measured by means of a Dutch translation of the CETI (Lomas et al., 1989), which is a 16-item visual analog scale scored by patients with aphasia and their relatives. After the treatment all patients were given a written non-standardized questionnaire regarding their satisfaction. They had to answer six questions on a seven-point Likert rating scale. The questions were about (1) the satisfaction of participation, (2) whether or not they would participate a second time, (3) the feasibility and the pleasantness of intensive treatment and (4) the preference of an intensive treatment above a nonintensive treatment. The ANELT and the CETI both measure verbal communication. They differ in that the ANELT is a standardized test for verbal communication, consisting of ten verbal scenarios to be answered by the aphasic patient. The verbal responses are rated for informational content on a 0-5 rating scale. Since in severe aphasia there might be a difference between the judgments of verbal communicative ability between experts and relatives (De Jong-Hagelstein, Kros, Lingsma, Dippel, Koudstaal, Visch-Brink, 2012) we also administered the CETI. The CETI is a subjective rating scale filled in by the patient as well as by their relatives.

Patient scores on the language tests are summarized in tables IV, V and VII.

2.5 Statistical analysis

Because of the small sample size, a non-parametric statistical analysis (i.e. Mann-Whitney test or Wilcoxon test) was carried out in addition to the parametric statistical analysis of the linguistic data. Only the parametric analysis is reported here because there was no difference

with the non-parametric tests. Differences in mean scores between groups on the ANELT and CETI were compared by means of independent-samples two-tailed t-tests. The improvement on the ANELT, the CETI, and AAT (T-transformed raw scores on 5 subtests), was measured by means of a paired-samples two-tailed t-test. The effect size (Cohen's d) was derived from within-group comparisons of the pre- and post-difference mean score from each treatment (Cohen, 1988). Critical changes in raw scores are discussed on an individual basis for all measurement outcomes. The AAT and BNT scores and the results on the subtests of the SAT and the PALPA are reported individually and evaluated based on the change before and after treatment.

3. RESULTS

Verbal communication in everyday life as measured by the ANELT (Blomert et al., 1995) showed a critical change in raw scores for 6 out of 9 (C2, C4, C5, B1, B2 and B3) participants (see shaded areas in Table IV). There was a significant improvement for both groups combined (mean improvement=11.8; $t(8)=6.00$, $p<.001$); improvement was smaller in the CIAT group (mean improvement=6.2; $t(4)=3.62$, $p=0.022$, $d=1.62$) than in the BOX group (mean improvement=8.2; $t(3)=4.99$, $p=0.015$, $d=2.50$). This difference was not statistically significant ($t(7)=-0.85$, $p=0.426$). However, it is important to notice that the significant difference in the prescores ($t(7)=3.40$, $p=0.011$), where patients of the BOX group started with a significantly lower score on the ANELT than the patients of the CIAT group, could have influenced improvement.

Insert* Table IV *here please

Verbal communication in everyday life was also measured by means of the CETI (Lomas et al., 1989) showed a critical change in raw score for 4 out of 9 (C4, B1, B2 and B3) participants (see Table IV). The relatives of the participants indicated that the effectiveness of the patients' communication had significantly improved after treatment (mean improvement=11.8, $t(7)=3.02$, $p=0.019$) for both treatment groups combined. No statistically significant difference in improvement after treatment was found between CIAT and BOX therapy ($t(6)=1.01$, $p=0.332$). When comparing pre- and postscores for both groups separately, however, no statistically significant difference was found in the CIAT group (n=5) ($t(4)=1.47$, $p=0.216$, $d=0.66$), while in the BOX group (n=3) the improvement was significant ($t(2)=7.40$, $p=0.019$, $d=4.27$). In addition, the pre- and postscores of the BOX group were higher than the pre- and postscores of the CIAT group on the CETI. Although the difference between the prescores of both groups did not reach statistical significance ($t(6)=1.69$, $p=0.142$), the difference between the postscores did ($t(6)=-2.93$, $p=0.026$).

Insert* Table V and VI *here please

Regarding the impairment-focused assessments, all participants (n=9) achieved a critical change in raw score as defined by the AAT (Graetz et al., 1992) on at least one of the AAT subtests or subscales (see shaded areas in Table V). Both groups improved on four AAT language subtests, i.e. comprehension, repetition, naming and written language. Only the amount of progress differed: although none of the BOX patients showed a critical improvement in raw score, the improvement in the BOX group was significant ($t(3)=5.19$, $p=0.014$, $d=2.59$) on the comprehension task, but the progress of language production was not, i.e. repetition ($t(3)=0.85$, $p=0.457$), naming ($t(3)=1.48$, $p=0.235$) and written language ($t(3)=1.46$, $p=0.239$) (Table VI). For the CIAT group the opposite was observed: the

improvement on the comprehension task did not reach significance ($t(4)=1.43$, $p=0.226$), but these participants scored well on language production, i.e. repetition ($t(4)=3.00$, $p=0.04$, $d=1.34$), naming ($t(4)=5.10$, $p=0.007$, $d=2.28$) and written language ($t(4)=4.24$, $p=0.013$, $d=1.90$) (Table VI). Only one CIAT participant (C5) showed a critical loss of score on the "Repetition Compounds" task (Table V). The CIAT group did very well on the Token Test (TT) ($t(4)=8.95$, $p=0.001$, $d=4.00$) and the Boston Naming Test (BNT) (Mariën et al., 1998) ($t(4)=6.12$, $p=0.004$, $d= 2.74$). The improvement of the BOX group did not reach significance on either test (TT: $t(3)=2.93$, $p=0.061$, BNT: $t(3)=2.42$, $p=0.094$). This, however, could be due to the small sample size (n=4). Small sample sizes require a very large effect size in order to reach significance. In the CIAT group this effect size was large enough to overcome the small sample size (n=5), in the BOX group, however, this was not the case. No differences were found between the two groups in the prescores on the TT and BNT (TT: $t(7)=0.90$, $p=0.399$; BNT: $t(7)=0.11$, $p=0.919$).

Insert* Table VII *here please

In order to evaluate the effectiveness of BOX and CIAT in patients with fluent aphasia, semantic and phonological measures were analyzed in more detail by means of various subtests of SAT and PALPA. Table VII summarizes mean progress on these measures after the two treatments. After BOX treatment, all four participants demonstrated critical gains on the subtests Semantic Word Association low imageability and three (B1, B2, B4) out of four on the subtest Auditory Synonym Judgment of the PALPA. However none of the four patients showed significant improvements on the SAT verbal. By contrast, only two (C3, C4; out of five) CIAT participants showed a change of two SDs on semantic measures (C3 on SAT verbal and C4 on PALPA semantic word association).

Considering the phonological measures, two (C2, C4) out of five CIAT participants demonstrated critical changes on both phonological tests (Table VII), i.e. on Auditory Lexical Decision and on Nonword Repetition. Two (B3, B4) out of four BOX participants showed critical gains on the Auditory Lexical Decision task (Table VII).

All participants expressed their satisfaction with the therapy and indicated that they would like to participate a second time. Patients unanimously agreed that intensive treatment is tolerable. All participants preferred a short period of intensive treatment over a prolonged treatment period. The BOX participants strongly agreed that their communication skills had improved after treatment, whereas agreement among CIAT participants was smaller.

4. DISCUSSION

Although only preliminary conclusions can be drawn from the relatively small sample size, this study demonstrates that chronic patients with a diagnosis of a moderate fluent aphasia after a left vascular lesion may significantly benefit from an intensive CIAT or BOX treatment in the chronic stage of recovery. Nine participants with a diagnosis of Wernicke aphasia or transcortical sensory aphasia with an underlying semantic and phonological deficit received intensive semantic treatment (BOX) or constraint-induced communicative treatment (CIAT). The two types of intervention differed in the theoretical perspective of the therapy (i.e. impairment-focused versus focus on CI-principles), the content (i.e. focus on semantics versus focus on verbal communication) and the nature of the interaction (i.e. one-to-one or group therapy). The therapy regime (duration, frequency and intensity) was identical in both groups and both groups received an intensive treatment of 30 hours over nine to ten weekdays. Meinzer et al. (2005), Maher et al. (2006), Barthel et al. (2008) and Berthier and Pulvermüller (2011) have demonstrated that treatment intensity has a positive effect on the

language and communication skills in a heterogeneous group of patients with chronic vascular aphasia. The findings of the present study are in line with these results and support the general behavioural effectiveness of a short-term intensive treatment approach in the chronic stage of aphasia.

In a homogeneous group, i.e. a chronic moderate fluent aphasia population, verbal communication (ANELT) showed a significant improvement for both groups, but improvement was smaller in the CIAT group than in the BOX group; nevertheless, the CIAT group scored better on language production (AAT-Repetition, AAT-Naming and BNT) than the BOX group. The more limited improvement on verbal communication (ANELT and CETI) might be in contradiction with the findings of Kirmiss and Lind (2011) who found more improvement in everyday communication after CIAT because turn taking and interactional behaviors are trained more intensively compared to purely carrying out written instructions after semantic treatment. It is important to notice that two factors could have influenced the improvement: (1) the significant difference in the prescores on the ANELT (e.g. scores of BOX group < scores of CIAT group); and (2) the way verbal effectiveness is measured. First, the smaller potential for improvement in the CIAT group possibly results in a lesser mean improvement, making a comparison between the two groups difficult. Second, the ANELT is a qualitative measure, looking at the verbal response as a whole, whereas a linguistic analysis, a quantitative detailed description of parameters such as the type token ratio and mean length of utterance of the ANELT responses might have been more sensitive to detect changes in verbal effectiveness over time (Doesborgh et al., 2004; Grande et al., 2008; Ruiter, Kolk, Rietveld, Dijkstra & Lotgering, 2011). With the CETI, however, no statistically significant improvement was found for the CIAT group. In contrast, the BOX group did improve significantly on the CETI even though the prescores of the BOX group on

the CETI were higher than those of the CIAT group, resulting in significant higher postscores in the BOX group than in the CIAT group.

Regarding the impairment-focused assessments, all participants (n=9) improved on at least one of the AAT subtests or subscales, i.e. comprehension, repetition, naming and written language (AAT). Only the amount of progress differed: the improvement in the BOX group was significant on the comprehension task, but the change in language production was not. For the CIAT group the opposite was true: no significant improvement on comprehension, while a significant improvement on language production was noted. A significant improvement was noted for the CIAT group, both on the TT (an aphasia severity scale) as on the BNT (a confrontation naming test), but not for the BOX group. This, however, could be due to the small sample size. Small sample sizes require a very large effect size in order to reach significance. More in-depth linguistic analysis (PALPA and SAT) showed that intensive task-oriented cognitive linguistic treatment of a specifically impaired linguistic level (BOX, i.e. a purely semantic treatment) in a chronic fluent aphasia population led to a significant improvement on two semantic measures (Semantic Word Association low imageability and Auditory Synonym Judgment) for almost all BOX participants (B1, B2 and B4, see Table VII). By contrast, only two (out of five) CIAT participants critically improved on semantics (C3 and C4). For phonology, two out of five CIAT (C2 and C4) participants showed significant improvement on both phonological tests, whereas in the BOX group improvement was seen on only one phonological subtest (Auditory Lexical Decision) in two out of four participants (B3 and B4). These linguistic results are in line with the results of Barthel et al. (2008), who emphasized that treatment effects were best achieved by specific and intensive treatment. The results are also in agreement with the findings of previous cognitive linguistic studies (Visch-Brink et al., 1997; Doesborgh et al., 2004) which reported a significant

influence on semantics but not on phonology after pure semantic treatment. The results also meet neurobiological principles of use-dependent learning whereas intensity as well as specificity of treatment affects improvement (Maher et al., 2006). Intensity has been reported in the literature to be an important factor in the outcomes of aphasia rehabilitation (e.g. Bhogal et al., 2003). However, intensity alone cannot explain the positive differences between the two groups' performance, because intensity was controlled. These results demonstrate that intensity of treatment as well as specificity of treatment could influence therapy outcome. In the BOX group lexical semantic skills, i.e. the underlying linguistic skill of comprehension, were trained. In the CIAT group, however, treatment focused on forced use of spoken language so that phonology, i.e. the underlying linguistic skill of language production, was trained. Kleim and Jones (2008) reported that treatment driven by a specific brain function can lead to an enhancement of that function.

In general, it was demonstrated that both types of therapy (CIAT and BOX) have a positive effect on verbal communication in chronic fluent aphasia. However, three out of nine (C1, C3 and B4) patients failed to improve on verbal communication (ANELT-results). These three patients did improve significantly on impairment-focused language tasks, i.e. naming (AAT-naming and BNT). This might be due to the fact that a naming test is less complicated than a communicative test in terms of the load on the language system and other cognitive functions. A naming test requires a straightforward word-level response, whereas a communicative test requires a coherent discourse-level response. A naming test might be less challenging for the cognitive system (the visual stimulus is the starting point of the clearly defined response), whereas a communicative test is influenced by auditory working memory (the patient has to memorize the instruction as well as the scenario) and by executive functioning (the patient has to consistently structure his answer and has to delineate his response).

Besides the small sample size and the chosen outcome measures, some other limitations to the study should be taken into account: (1) previous treatment experience by the participants; (2) relevance of materials; (3) clinician's experience and (4) group versus single-patient setting. First, it is not known which therapy regimen (content or quantity) the participants have received before participating in this study. It is known that none of the nine participants had prior exposure to an intensive therapy program. As Holland, Greenhouse, Fromm and Swindell (1989) noted, previous treatment might be an influential factor on treatment outcome since the treatment might facilitate or speed up neural recovery processes. Second, Murray and Clark (2006) found that the degree of relevance of materials to the participant contributes to generalization. This factor was not examined in this study. Third, the CIAT and BOX treatment was given by seven different students, although these students received the same training and coaching, their experience, personality and way of shaping might have influenced the participants' outcome. The fact that students instead of professionals supervised the interventions should have no impact since several studies (Davis, Enderby & Bainton, 1982; Lesser, Bryan, Anderson & Hilton, 1986; Marshall et al., 1989; Meikle et al., 1979; Shewan & Kertesz, 1984; Wertz et al., 1986; Worrall & Yiu, 2000) found no differences in language improvement of patients with aphasia, when treatment was applied by trained laypersons or by professional therapists (Meinzer at al., 2007). Fourth, therapy in a single-patient setting is more intensive than in a group setting, where practice time is divided among the group members (Berthier & Pulvermüller, 2010). In this study CIAT-participants received as much individualized cueing as necessary for a successful expression (no detailed records were kept to count the exact minutes), whereas BOX-participants alternated between working 30 minutes by themselves and 30 minutes with the therapist. This might have caused a more intensive experience for the BOX group.

The question remains whether a specific treatment (BOX or CIAT) delivered under different conditions (i.e. varying the intensity schedule, quantity of treatment, aphasia population/ linguistic impairments, involving relatives) would still yield positive outcomes. Some suggestions for further study can be summarized as follows: (1) How can the delivery of therapy be restructured to enhance the learning effect (e.g. is an intensive treatment schedule beneficial in the subacute phase); (2) Which type of aphasia responds best to intensive treatment (e.g. is an intensive phonological treatment in an individual with conduction aphasia more useful than CIAT-therapy (Szaflarski et al., 2008; Goral & Kempler, 2009)); (3) Which linguistic process should be intensively trained (e.g. will an intensive, phonologically based therapy in fluent aphasia also significantly improve verbal communication); and (4) What are the most appropriate outcome measures to assess treatment gains (e.g. is more attention to conversation screening and analysis as useful as in-depth assessment of the impact on verbal communication (DiFrancesco et al., 2012))?

We can conclude based on this explorative study that (1) intensive treatment has a significant effect on language and communication skills; (2) an intensive semantic treatment (BOX) results in selective treatment effects and a more pronounced improvement of verbal communication when compared to CIAT.

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Appendix

Detailed description of the constraints used in CIAT-training

Material constraints

All words represented by pictures of objects and actions (n=450) were classified for lexical frequency (high, middle and low frequency words) according to the database CELEX (Centre for Lexical Information; Bayen, Piepenbrock, & Van Rijn, 1993). Because of the moderate severity of language impairment in both CIAT groups, the participants almost exclusively practiced with low frequency picture cards (n=287). In the first sessions, only simple black-and-white line drawings of objects (n=249) were used. These drawings were taken from an Internet database (Szekely et al., 2004). Later on, colored pictures of objects from different semantic categories or themes, action cards, sentences cards (n=173) (internet database 'Imagine Symbols', 2004) and pictures with minimal pairs (n=28) were introduced. Thus, the therapist triggered a more advanced communication by means of (1) decreasing word frequency, (2) introducing coloured pictures from the same semantic category or theme, (3) using action or sentence cards and (4) requesting the exact pronunciation by using cards of phonetically minimal pairs.

Shaping and rules constraints

In the first session, participants were allowed to use any relevant verbal expression to obtain a particular card. The therapist provided as much cueing as necessary for a successful expression. Cueing strategies that were used consisted of: semantic cueing, phonological cueing, selecting, repeating or a reminder/visual cueing. These verbal expressions and cueing strategies were gradually constrained by (1) the introduction of explicit rules and (2) shaping and modelling (i.e. encourage increasing complexity of verbal responses). The rule of constraining allows the

players (1) to use the names of the co-players, (2) to use politeness rules and (3) to use more complex verbal expressions. To encourage the self cueing capacities of the patients in a communication setting and to introduce the use of more complex verbal expressions, the "questioner" was sometimes asked to give only a description of the object. The "receiver" was expected to name the object. Following the shaping principle, the cueing strategies were gradually reduced. Finally, the participants were encouraged to communicate without any help.

Reinforcement contingencies

Because we composed groups based on a similar degree of linguistic impairment, the rules and shaping principles could be performed on a group basis. Everyone could practice with the same rules and constraints.

Detailed description of the exercises used in BOX-training

There are eight different types of exercises: I Semantic Categories; II Syntagmatic and Paradigmatic Relationship; III Semantic Gradiation; IV Adjectives and Exclamations; V Part-Whole Relationship; VI Anomalous Sentences; VII Semantic Definition; VIII Semantic Context.

Most of the exercises contain three levels of difficulty:

- Word choice: imageability, frequency, word length, and abstractness were considered.
- Number of distractors: in general the level of difficulty increases by adding more distractors.
- Semantic relatedness: there are mostly unrelated distractors at the easy level, and only related distractors at the most difficult level.
- Ambiguity: incorporated in the difficult level are ambiguous words; this task is to survey both word meanings at the same time.

1 **Some examples of exercises** (Visch-Brink et al., 1997)

LEVEL 1	**LEVEL 2**	**LEVEL 3**
I Semantic Categories Postcard *Cigar* Bill	Comma *Number* Question mark Semi-colon parentheses	Greatness Superiority Importance Power *Motivation* Authority
II Syntagmatic and Paradigmatic Relationship CRIPS: *popcorn* or towel Let's have something to go with our drinks	THEATRE: *musical* or home movie It appears that the show is sold out.	INTERPRETER: actor, *translator* or courier The Russian ambassador is coming to Holland.
III Semantic Gradation *SPRING* or AUTUM *Blossom* *cleaning* Mushroom chestnut *First cuckoo* September		
IV Adjectives and Exclamations		

The boy from next door is playing in the mud. - *The boy from next door is dirty.* - The boy from next door is clean.	**That piano makes a terrible noise.** - The piano is white. - The piano is new. - *The piano is out of tune*.	**I 've got my driver's licence!** - Oh dear. - *Congratulations!* - Is that so?
V Part whole relationship The towels are in **the linen-cupboard**. *Dishcloth* Lawn mower *handkerchief*	That painting has a nice **list.** *Portrait* *Watercolour* film	A cat's **tail.** *Frock* Dress Coat

Table I Demographic and neurological data

		Treatment Group	Age (years)	Sex	Handedness	Education (years)	Duration of Aphasia (months)	Etiology	Lesion site	Classification of aphasia	Severity of aphasia pretest
Case	C1	CIAT	73	F	R	8	17	I	L	TC sensory	Moderate
	C2	CIAT	65	F	R	12	70	I	L	Wernicke	Moderate
	C3	CIAT	69	F	R	15	25	H	L	TC sensory	Moderate
	C4	CIAT	55	M	L	15	138	I	L	Wernicke	Moderate
	C5	CIAT	54	M	R	17	56	I	L	Wernicke	Moderate
		Mean (SD)	63 (8)			12 (6)	61 (48)				
	B1	BOX	60	M	R	13	61	H	L	Wernicke	Moderate
	B2	BOX	76	M	R	12	26	I	L	Wernicke	Moderate
	B3	BOX	81	M	R	15	82	I	L	TC sensory	Moderate
	B4	BOX	68	M	R	12	37	I	L	Wernicke	Moderate
		Mean (SD)	71(9)			13 (1)	52 (25)				

Note. C=CIAT, B=BOX; SD=Standard Deviation); F=female, M=male, R=right, L=left, I=ischemic, H=hemorrhagic), TC=transcortical.

Table II Therapy schedule in minutes BOX 1, BOX 2 and CIAT

Therapy schedule BOX 1	Therapy schedule BOX 2	Therapy schedule CIAT
A: 30 Therapy session	A: 30 Individual work session	45 Therapy Session
B: 15 Individual work session	B: 15 Therapy session	
Pause	**Pause**	**Pause**
A 30 Individual work session	A 30 Therapy session	45 Therapy Session
B 15 Therapy session	B 15 Individual work session	
Pause	**Pause**	**Pause**
A 30 Therapy session	A 30 Individual work session	45 Therapy Session
B 15 Individual work session	B 15 Therapy session	
75 Therapy session	60 Therapy session	135 Therapy session
60 Individual work session	75 Individual work session	

Note. A=first part of 45 min (30 min), B=last part of 45 min (15min).

Table III Test procedure

To establish functional lateralization of the brain	- Handedness Inventory
To measure visuoperceptual problem solving	- Raven Colored Progressive Matrices
To establish an overall cognitive linguistic profile	- Aachen Aphasia Test - Boston Naming Test
To measure semantic outcomes	- PALPA Synonym Judgment test - PALPA Semantic Word Association of low imageability words - Visual Semantic Association Test - Verbal Semantic Association Test
To measure phonological outcomes	- PALPA Non-word Repetition - PALPA Auditory Lexical Decision
To measure verbal communication and social validation	- Amsterdam, Nijmegen Everyday Language Test - Communicative Effectiveness Index
To evaluate satisfaction	- Written, non-standardized subjective rating scale

Table IV Individual case data: ANELT and CETI pre- and post therapy, and improvement

		ANELT Max 50			CETI Max 100		
		pre	post	I	pre	post	I
CIAT	C1	41	45	4	54.7	61.0	6.3
	C2	35	46	11	46.1	52.4	6.3
	C3	38	39	1	43.4	43.4	0.0
	C4	32	40	8	25.0	56.2	31.2
	C5	40	47	7	40.0	39.2	-0.8
	Mean	37.2	43.4	6.2	41.9	50.5	8.6
	(SD)	(3.7)	(3.6)	(3.8)	(10.9)	(9.0)	(13.1)
BOX	B1	29	37	8	44.1	61.5	17.4
	B2	33	42	9	56.7	69.6	12.9
	B3	30	42	12	64.2	85.0	20.8
	B4	26	30	4	(89.4)	/	/
	Mean	29.5	37.8	8.3	55	72.0	17.0
	(SD)	(2.9)	(5.7)	(3.3)	(10.2)	(12.0)	(4.0)

Note. SD=Standard Deviation, I=Improvement; C=CIAT, B=BOX; Shaded areas indicate on an individual basis a critical change in raw score as defined by the ANELT (≥7 points) or by the CETI (≥10 points).

Table V Individual case data**:** Aachen Aphasia Test (Token Test, Comprehension, Repetition, Naming, Written Language) and Boston Naming Test (BNT) raw scores pre- and post- therapy

	CIAT-group										BOX-group									
	C1		C2		C3		C4		C5		Mean (SD)		B1		B2		B3		B4		Mean (SD)	
	pre	post	pre	post	pre	post	pre	post	pre	post			pre	post	pre	post	pre	post	pre	post		
Token Test (max 50)	29	20	28	18	38	28	39	24	32	17	33.2 (5.1)	21.4 (4.6)	29	20	24	13	39	34	27	26	29.8 (6.5)	23.3 (8.9)
Comprehension (max 120)	81	92	79	87	88	86	87	96	104	100	87.8 (9.8)	92.2 (5.9)	103	110	100	113	66	83	104	113	93.3 (18.2)	104.8 (14.6)
Repetition (max 150)	144	148	119	124	132	136	116	130	105	108	121.2(16.4)	129.2 (14.8)	117	120	136	143	145	143	95	94	123.3(22.2)	125.0(23.3)
Compounds (max 30)	29	29	22	22	18	23	20	26	17	10	21.2 (4.8)	22.0 (7.2)	18	16	26	29	29	29	9	12	20.5 (9.0)	21.5 (8.8)
Sentences (max 30)	27	29	14	16	24	23	12	18	9	12	17.2 (7.8)	19.6 (6.6)	13	16	25	25	28	26	9	11	18.8 (9.2)	19.5 (7.2)
Naming (max 120)	93	96	96	102	66	75	90	99	99	111	88.8 (13.2)	96.6 (13.3)	86	105	96	87	48	57	77	104	76.8 (20.7)	88.3 (22.4)
Color (max 30)	27	27	28	28	16	25	28	27	30	30	25.8 (5.6)	27.4 (1.8)	30	30	23	18	14	15	30	30	24.3 (7.6)	23.3 (7.9)
Compounds (max 30)	25	22	20	22	12	12	23	24	19	28	19.8 (5.0)	21.6 (5.9)	17	26	25	22	10	12	16	28	17.0 (6.2)	22.0 (7.1)
Sentences (max 30)	16	21	21	23	18	18	13	25	20	23	17.6 (3.2)	22.0 (2.6)	14	20	24	20	7	13	10	16	13.8 (7.4)	17.3 (3.4)
Written Language (max 90)	84	87	82	84	67	72	81	82	66	70	76.0 (8.7)	79.0 (7.5)	82	85	76	73	79	85	65	74	75.5 (7.4)	79.3 (6.6)
To dictation (max 30)	26	27	28	27	23	29	26	25	11	17	22.8 (6.8)	25.0 (4.7)	27	27	23	20	26	27	15	21	22.8 (5.4)	23.8 (3.8)
BNT (max 60)	30	45	33	39	7	17	37	44	44	54	30.2 (14.0)	39.8 (13.8)	37	46	46	45	0	19	33	49	29.0 (20.1)	39.8 (13.9)

Note. Shaded areas indicate on an individual basis (1) a critical change in raw score as defined by the AAT (Token Test=8, Comprehension=22, Repetition=15 (compounds=7, sentences=7), Naming=17 (colors=10, compounds:10, sentences=7), Written Language=12 (writing to dictation=8)) or (2) a change in score of $\geq$ 2SD from the gender, age and education adjusted mean normal performance on the BNT. Token Test is an error score.

Table VI t- and p-values of the comparison (paired t-test) between the pre- and postscores on the subtests of the Aachen Aphasia Test (Comprehension, Token Test, , Repetition, Naming, Written Language) and on the Boston Naming Test of the CIAT- and the BOX-group

	CIAT-group		BOX-group	
	t(4)-value	p-value	t(3)-value	p-value
Comprehension	1.43	0,226	5.19	0.014
Token Test	8.95	0.001	2.93	0.061
Repetition	3.00	0.040	0.85	0.457
Naming	5.10	0.007	1.48	0.235
Written Language	4.24	0.013	1.46	0.239
Boston Naming Test	6.12	0.004	2.42	0.094

Note. Shaded areas indicate a significant difference in pre- and postscores according to the paired t-test ($p \leq 0.05$).

Table VII Individual case data: Raw scores and mean scores pre- and post therapy on semantic and phonological measures (n=9)

		Semantic Measures			Phonological Measures	
		Verbal Semantic Word Association (SAT) Max 30	Semantic Word Association Low Imageability (PALPA) Max 15	Auditory Synonym Judgment (PALPA) Max 60	Nonword Repetition (PALPA) Max 30	Auditory Lexical Decision (PALPA) Max 160
		pre post	pre post	pre post	pre post	pre post
Case	C1	24 22	6 7	47 49	28 27	149 148
	C2	21 24	14 13	51 51	18 21	131 140
	C3	18 28	6 7	54 52	27 29	156 156
	C4	22 25	8 10	52 53	18 27	129 152
	C5	30 27	13 12	57 57	21 22	157 160
	Mean (SD)	23.0 25.2 (4.5) (2.4)	9.4 9.8 (3.8) (2.8)	52.2 52.4 (3.7) (3.0)	22.4 23.4 (4.8) (6.9)	144.4 151.2 (13.5) (7.7)
	B1	27 28	12 14	52 59	28 26	159 154
	B2	23 27	8 10	49 55	24 25	141 140
	B3	13 12	3 6	46 46	26 28	139 144
	B4	27 30	12 14	54 58	3 4	124 136
	Mean (SD)	22.5 24.2 (6.6) (8.3)	8.7 11 (4.3) (3.9)	50.2 54.5 (3.5) (5.9)	20.2 20.7 (11.6) (11.2)	140.75 143.5 (14.3) (7.7)

Note. Shaded areas indicate on an individual basis a critical change in raw score on the Semantic Association Test (≥6 points), and a change in score of ≥ 2SD from the mean on the Semantic word association for low imaginability words (≥2 points) on the Auditory synonym judgment (≥3 points), the Repetition of nonwords (≥3points) and the Auditory lexical decision (≥5 points).